

Lymph Node Staging in Colorectal Cancer: Revisiting the Benchmark of at Least 12 Lymph Nodes in R0 Resection

Jinru Shia, MD, Hangjun Wang, MD, Garrett M Nash, MD, David S Klimstra, MD

Since the development of Dukes' classification system for colorectal carcinoma in the 1930s by English pathologist Cuthbert Dukes,¹ which emphasized the importance of lymph node involvement, the status of lymph nodes in a colorectal cancer resection specimen has remained the most powerful indicator for prognostication and management.²⁻⁴ The most important components in lymph node staging include the presence or absence of metastasis in lymph nodes and the total number of lymph nodes examined. The assessment of both components, however, can be influenced by many factors, and how best to carry out the assessment has been an evolving topic. This review aims at analyzing the various factors that can potentially influence lymph node assessment, and how such influences can impact the clinical application of the current benchmark requirement of at least 12 lymph nodes for a colonic or rectal cancer resection.

IMPORTANT COMPONENTS IN LYMPH NODE STAGING

The first important component in lymph node staging is the presence or absence of metastatic carcinoma. Dukes was among the first to recognize this significance, and he started staging colorectal cancers based primarily on lymph node metastasis back in the 1930s.^{1,5} Since then, the status of lymph nodes in cancer staging has remained highly visible.² Although the coding system may have changed from Dukes' A, B, C, D into TNM I, II, III, IV, the essence of every system has hinged on whether any positive lymph node is present. Numerous studies have attested to the validity of such a staging strategy.⁶⁻¹⁰

Over the last 2 decades, the number of lymph nodes removed and examined in a colorectal cancer resection has grad-

ually emerged as another important component in lymph node staging.^{4,11-16} Many studies have arrived at 2 basic conclusions. One, a larger number of lymph nodes is associated with an increased likelihood of identifying lymph node metastases.^{7,17} Two, the number of lymph nodes examined is associated with prognosis, with outcomes association being significant in both the node positive and node negative groups.^{4,11} Indeed, when Chang and colleagues¹⁸ systematically reviewed 17 studies from 9 different countries involving 61,731 patients, an association between the number of lymph nodes in both node negative (stage II) and positive (stage III) colon cancers and survival was demonstrated. As a result of such studies, the prevailing sentiment has been that a certain minimum number of nodes should be examined before lymph node staging can be considered adequate.

Thus, in 1991, based primarily on 2 studies^{19,20} that suggested 12 or 13 lymph nodes may serve as the appropriate minimum recovery number, a Working Party Report to the World Congresses of Gastroenterology reached a consensus recommendation that at least 12 lymph nodes must be sampled to adequately stage a patient.²¹ Since then, a surge of studies has served to provide further evidence that empowers this seemingly trivial issue in our practice. In 2001, the National Cancer Institute recommended that at least 12 lymph nodes be harvested and examined to properly define a colorectal cancer as node negative.²² In 2007, the harvest of at least 12 lymph nodes was endorsed by the National Quality Forum as a standard quality indicator for segmental colorectal cancer resection specimens.²³ Similarly, the 7th edition of the American Joint Committee on Cancer (AJCC) staging manual pointed out that "it is important to obtain at least 10-14 lymph nodes in radical colon and rectum resection in patients without neoadjuvant therapy."

However, concerns exist about whether the number 12 is indeed the most appropriate minimum recovery number. The methodology of the 2 studies^{19,20} that constituted the major data source for the development of this benchmark number has been criticized, particularly for its inability to evaluate the impact of terminating a lymph node recovery on the identification of lymph node metastases. Indeed, subsequent studies found it difficult to find a number above which the detection of lymph node metastasis plateaus.^{11,14}

Disclosure Information: Authors have nothing to disclose. Timothy J Eberlein, Editor-in-Chief, has nothing to disclose.

Received October 10, 2011; Revised November 16, 2011; Accepted November 23, 2011.

From the Departments of Pathology (Shia, Wang, Klimstra) and Surgery (Nash), Memorial Sloan-Kettering Cancer Center, New York, NY.

Correspondence address: Jinru Shia, MD, Department of Pathology, Memorial Sloan-Kettering Cancer Center, 1275 York Ave, New York, NY 10065. email: ShiaJ@Mskcc.org

Abbreviations and Acronyms

BMI	=	body mass index
LNR	=	lymph node ratio
MSI	=	microsatellite instability
MSI-H	=	microsatellite instability-high

FACTORS AFFECTING LYMPH NODE YIELD IN COLORECTAL CANCER RESECTIONS

The lymph node yield is subject to a variety of factors,^{16,24-30} and many resection specimens have a yield of lymph nodes lower than 12, with only 48% of the cases meeting the benchmark in one study.²⁶ The influencing factors can be broadly categorized as those related to the 3 major components involved in the lymph node retrieval process: the patient, the surgeon, and the pathologist.

The patient

The patient contributes to the yield of lymph nodes in a given colorectal cancer resection through individual characteristics such as age, sex, and body mass index (BMI), as well as through tumor-related factors such as location, size, and pathologic stage.

The impact of the patient's age on lymph node retrieval in a colorectal cancer resection has been examined in a number of studies. Most agree that colorectal cancer resections yield fewer lymph nodes in older patients. One recent study based on the Surveillance Epidemiology and End Results (SEER) database on nonmetastatic colon cancer patients diagnosed from 1992 to 2004 indicated that the mean lymph node yield decreased with increasing age and the proportion of patients meeting the 12-lymph node benchmark declined with each 5-year incremental age group.³¹ Another analysis based on SEER database from 1995 to 2004 showed that for every 10-year incremental increase in age, there was an average reduction of 9% in lymph node harvest in colorectal cancer resections.³² These are intriguing observations. Various mechanisms could be speculated. For example, older age may be associated with a process of involution and therefore a reduction in number or size of lymph nodes, and smaller nodes are harder for the pathologists to identify. It is also possible that there are more comorbidities in older patients, so there would be a tendency for the surgeons to perform a less extensive dissection.

The impact of both sex and BMI has been examined. Although a number of studies suggest no relationship between sex and lymph node yield,^{27,28,30,32,33} some report a positive association, with females more likely to have a higher yield.^{26,30} Similarly, whether an association exists between BMI and lymph node yield remains an open question. Some studies

indeed demonstrate an inverse relationship, with increased BMI being associated with a lower lymph node yield. Such a relationship has been shown in both nontreated³² and post-neoadjuvant rectal cancer resections.³⁴ Other studies, however, failed to demonstrate any association. Linebarger and associates³⁵ studied 401 colonic cancer resections and suggested that obesity resulted in increased technical difficulty with longer operative time, but did not affect the adequacy of lymph node harvest, regardless of surgical approach (open vs laparoscopic).

The characteristics of the patient's tumor itself appear to exert a significant effect on the lymph node status. Features shown to influence lymph node yield include tumor size, pT stage, tumor location, and very importantly, neoadjuvant therapy. Furthermore, it has been shown that the DNA mismatch repair status influences the yield of lymph nodes in colorectal cancer resections.

The effect of tumor size on lymph node yield has been shown in many studies. Chou and coworkers³² demonstrated that for every 1-cm increase in tumor size, there was an average increase of 2% to 3% in the number of lymph nodes identified, 2% for colon and 3% for rectum. Others have shown that a tumor of more than 4 cm was associated with 5.5 more lymph nodes than a tumor less than 4 cm.³⁶ In addition, a more advanced pT stage had also been associated with a higher lymph node yield.^{37,38}

The association of tumor location with lymph node yield has been a consistent finding.^{15,27,32} Tumors located in the ascending colon/hepatic flexure, on average, have 34% more lymph nodes retrieved than those in the sigmoid or rectosigmoid region.³² It is likely that this at least in part reflects the fact that the right colectomies resect longer segments of bowel and therefore have more fat and mesentery attached.²⁷

Notably, the rectum seems to differ from the colon conspicuously in issues related to lymph nodes. First, the fact that rectal cancer resections tend to have fewer lymph nodes identified has been well demonstrated.^{32,39} That lymph nodes in the rectum tend to be smaller, as observed by Dworak,⁴⁰ may be a contributing factor. The intriguing observation is that despite a lower overall count, the rate of positive lymph nodes tends to be higher. Wang and coauthors³⁹ analyzed 2,340 patients with R0 colorectal cancer resections, 1,314 rectal and 1,026 colonic, with none receiving neoadjuvant therapy, and found a significantly higher proportion of positive lymph nodes in the rectal group (41.4% vs 35.5%, $p = 0.004$). Second, rectal cancer resections after neoadjuvant therapy have even fewer lymph nodes. Several studies have shown that neoadjuvant therapy reduces lymph node counts in resection specimens.^{36,38,41} This effect has been directly associated with the

Download English Version:

<https://daneshyari.com/en/article/4293829>

Download Persian Version:

<https://daneshyari.com/article/4293829>

[Daneshyari.com](https://daneshyari.com)